

REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments, remarks and enclosures herewith.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 1, 3, 4, 6-17, 20-26, 28-32, 35-40, 43 and 45 are pending in this application. Claims 3, 7 and 8 have been withdrawn from consideration as allegedly being drawn to non-elected subject matter. Applicants reserve the right to pursue the withdrawn claims in this or future applications. Claims 1 and 45 have been amended, and claim 43 has been cancelled without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

Claims 1 and 45 have been amended to recite ‘comprising removing the cornified epithelium from the skin of the animal and contacting the outer most layer of the exposed skin of the animal with a live bacterial vector’ (claim 1) or “a live gram negative bacterial vector” (claim 45). Support for removal of the cornified epithelium may be found, for example, in paragraph 116 of the specification as originally published. Support for the use of live bacteria may be found, for example, in paragraph 20 of the specification as originally published. Support may also be found in paragraph 77 of the specification, which recites “Specifically, the bacterial vectors, according to the present invention, are preferably gram-negative bacteria which can invade mammalian hosts”. Support for the recitation of gram negative bacteria may be found in paragraph 11 of the specification as originally published. Applicants submit that one skilled in the art would agree that for an organism to actively “invade” a host, said organism must be living.

No new matter is added.

It is respectfully submitted that the claims, herewith and as originally presented, are patentably distinct over the art, and that those claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The remarks made herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, the amendments and remarks herewith are made simply for clarification and to round out the scope of protection to which Applicant is entitled.

II. THE 35 U.S.C. § 102 REJECTIONS ARE OVERCOME

Claims 1, 9-14, 21-22, 25-26, 28-32, 38 and 43 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Roop *et al.* Claims 1, 9-14, 21-22, 25-26, 28-32, 38 and 43 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Carsen *et al.* Applicants respectfully traverse.

It is respectfully submitted that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Bariant Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

The Examiner contends that Roop *et al.* relates to the use of a plasmid vector for inducing an immunological response and notes that “a plasmid vector can be considered to be a ‘bacterial vector’ because a plasmid vector contains bacterial sequences and it is propagated and selected in bacteria using a selective marker.” Office Action at 4.

Although Applicants do not agree with the Office Action, in the interest of expediting prosecution, claims 1 and 45 amended herein recite a live bacterial vector (claim 1) or a live gram-negative bacterial vector (claim 45). Neither Roop *et al.* nor Carsen *et al.* teach or suggest the use of live bacteria vectors. Further, claims 1 and 45 amended herein recite a non-invasive method comprising removing the cornified epithelium from the skin of the animal and contacting the outer most layer of the exposed skin of the animal with a live bacterial vector. Neither Roop *et al.* nor Carsen *et al.* teach or suggest removing the cornified epithelium or applying the vector to the outermost layer of the exposed skin. Thus, neither reference meets every limitation of the claimed invention and cannot be considered proper references under Section 102.

Accordingly, reconsideration and withdrawal of this Section 102(e) rejection are respectfully requested.

III. THE 35 U.S.C. §103 REJECTIONS ARE OVERCOME

Claims 1, 4, 6, 15-17, 20, 23-24, 35-37, 40 and 43 were rejected under 35 U.S.C. §103(a)

as allegedly being unpatentable over Powell *et al.* or WO 01/89535 A1 in view of Roop *et al.* Applicants respectfully traverse.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Although a teaching, suggestion, or motivation to combine is no longer rigidly required for a finding of obviousness, it remains the primary guarantor against a non-statutory hindsight analysis. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): “The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification.” The requirement that for the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicant’s disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Furthermore, The Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: “[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727.

Applying the law to the instant facts, the references relied upon by the Office Action does not disclose, suggest or enable Applicants’ invention.

The Examiner contends that Powell *et al.* relates to infecting animal cells with ‘live invasive bacteria’ and further pertains to “intradermal and intramuscular” introduction of said bacteria. The Examiner also contends that WO 01/89535 relates to “bacterial blebs or minicells,” which according to the Examiner may be considered to be ‘a modified version of live bacterial cells,’ and that this references pertains to “intradermal and intramuscular” routes of administration. The Examiner further contends that Roop *et al.* discloses that “topical

administration of the vectors is advantageous”, and that it would have allegedly been obvious for one skilled in the art to modify the method of either Powell *et al.* or WO 01/89535 by topical application of live bacteria. Office Action at 5. Applicants respectfully disagree.

Turning first to the Powell *et al.* and the WO 01/89535 references, Applicants submit that both references pertain primarily to the use of “infect[ed] animal cells that are cultured *in vitro*,” and then the “*in vitro*-infected or the *in vitro*-enriched cells can then be introduced into animals intravenously, intramuscularly...” (See column 19, lines 36-49 of the Powell *et al.* publication, and note that WO 01/89535 recites similar language.) The claims of the present invention, as amended herein, recite a non-invasive method comprising “removing the cornified epithelium from the skin of the animal and contacting the outer most layer of the exposed skin of the animal with a live bacterial vector”. Both Powell *et al.* and WO 01/89535 further pertain to the use of invasive bacteria to infect the animal by “intravenous, intramuscular, intradermal, intraperitoneally, peroral, intranasal, intraocular, intrarectal, intravaginal, oral, immersion and intraurethral inoculation routes”. “See column 19, lines 50-55 of the Powell *et al.* reference, noting again that WO 01/89535 recites the same language.” Neither Powell *et al.* nor WO 01/89535 teach or suggest first removing the cornified epithelium from the skin and non-invasively administering live bacteria to the outermost layer of the exposed skin of an animal. And, neither reference provides any motivation or incentive to do so.

Turning now to Roop *et al.*, this reference does not teach topical administration of live bacterial vectors to the outermost layer of the skin, nor does it provide any motivation or incentive to do so. In fact, Roop *et al.* teaches away from the present invention by reciting the use of cell transformation methods, for example, liposomes, proteoliposomes, and DNA coupled to macromolecular complexes, which are typically used to introduce non-living vectors into a cell (see column 20, lines 39-44). Further, Roop *et al.* does not teach removing the cornified epithelium prior to administration of a vector.

Moreover, none of the cited references under the § 103 rejection indicate that there would be an expectation of success if one were to apply live bacterial vectors to the outmost layer of de-cornified skin. Applicants submit that the fact that neither Powell *et al.* nor WO 01/89535 teach topical application suggests that there was not an expectation that such a non-invasive method for application of live cells to an animal would prove effective. Likewise, while Roop *et al.* may relate to topical administration as a general method of delivery, there is no indication that

employing such a non-invasive method would be an effective route for delivery of live bacterial vectors to animals.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1, 29, and 39 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over either Carsen *et al.* or Roop *et al.* in view of either Alexander *et al.* or Li *et al.* Applicants respectfully traverse.

The Examiner contends that both Carsen *et al.* and Roop *et al.* pertain to the use of a plasmid vector for inducing an immunological response and notes that “a plasmid vector can be considered to be a ‘bacterial vector’ because a plasmid vector contains bacterial sequences and it is propagated and selected in bacteria using a selective marker.” Office Action at 6. As discussed above, claim 1 amended herein recites (1) a live bacterial vector, (2) a non-invasive method of administration comprising removing the cornified epithelium from the skin, and (3) application to the outermost layer of the exposed skin. Neither Carsen *et al.* nor Roop *et al.* teach or suggest the use of these elements. Therefore, neither reference may be combined with either Alexander *et al.* nor Li *et al.* to render the claimed subject matter *prima facie* obvious.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claim 45 was rejected under 35 U.S.C. § 103(a) as being unpatentable over either Powell *et al.* or WO 01/89535 A1 in view of Roop *et al.*, and further in view of Robinson *et al.* Applicants respectfully traverse.

As discussed above, the claims as amended herein recite a non-invasive method comprising removing the cornified epithelium from the skin of the animal and contacting the outer most layer of the exposed skin of the animal with a live bacterial vector. For the same reasons discussed above, none of Powell *et al.*, WO 01/89535 or Roop *et al.*, even when combined with Robinson *et al.*, teach or suggest the presently claimed invention, and none of the cited references demonstrate an expectation of success resulting from non-invasive administration of live bacterial vectors to the outermost layer of the de-cornified skin of an animal.

Accordingly, reconsideration and withdrawal of all rejections under 35 U.S.C. § 103(a) are respectfully requested.

IV. THE DOUBLE PATENTING REJECTION IS OVERCOME

Claims 1, 9-14, 21-22, 25-26, 28-31, 38-39 and 43 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-3 of U.S. patent No. 6,706,693. Claims 1, 4, 6, 9-17, 20-26, 28-32, 35-40 and 43-44 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-38 and 93 of co-pending Application Serial No. 10/346,021. Applicants will consider these rejections, including the possibility of filing a terminal disclaimer to obviate the rejections, upon the determination of allowable subject matter in the present application.

Claims 1, 11-13, 25-26, 28-32, 38-39 and 43 were provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1, 6-8, 20-21, 23-27 and 33-35 of co-pending Application Serial No. 10/116,963. Applicants believe that the elections of species between the applications will result the avoidance of this rejection upon the determination of allowable subject matter. Accordingly, this rejection will be considered at such time as the pending claims have otherwise been deemed allowable.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to further examination and/or allowance, an interview with the is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the rejections of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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